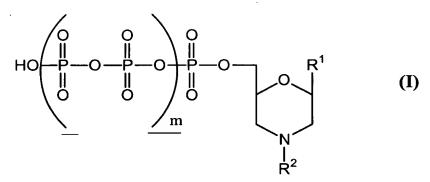
1. (Currently Amended) Process for manufacturing a 3'-labelled nucleic acid (DNA or RNA) fragment, which comprises the enzymatic incorporation of a nucleotide derivative having as precursor a compound of formula:

in which R¹ represents a nucleic base, m is 1 and R² is selected from the represents a group consisting of corresponding to one of the following formulae:

in which n is an integer ranging from 1 to 12 and R³ is selected from the a group consisting of derived from a label, a protein, an enzyme, a fatty acid or and a peptide, at the 3' OH end of the nucleic acid fragment.

2. (Currently Amended) Process for modifying a nucleic acid fragment by enzymatic incorporationing at the 3' end of the nucleic acid fragment a modified morpholino nucleotide having as precursor a compound corresponding to the formula:





in which R^1 represents a nucleic base, m is 1 and R^2 is selected from the group consisting of represents a group corresponding to one of the following formulae:

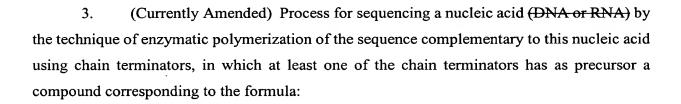
$$-(CH2)n-NH-R3$$

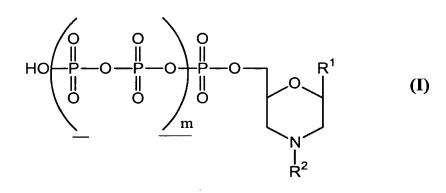
$$-(CH_2)_n$$
-CO-R³

$$-(CH_2)_n-SR^3$$

and
$$-(CH_2)_n$$
-OR³

in which n is an integer ranging from 1 to 12 and R³ is selected from the group consisting of represents a compound chosen from photo-crosslinking agents, fatty acids, hydrophobic peptides, antibodies, enzymes and fluorophores.







Application Serial No. 09/914,221 Attorney's Docket No. 025219-342

in which R¹ represents a nucleic base, m is 1 and R² is selected from the represents a group consisting corresponding to one of the following formulae:

$$-(CH_{2})_{n}-NH_{2} -(CH_{2})_{n}-SH$$

$$-(CH_{2})_{n}-COOH -(CH_{2})_{n}-NH-R^{3} -(CH_{2})_{n}-SR^{3}$$

$$-(CH_{2})_{n}-CO-R^{3} -(CH_{2})_{n}-OR^{3}$$

in which n is an integer ranging from 1 to 12 and R³ is selected from the group consisting of a group derived from a label, a protein, an enzyme, a fatty acid or and a peptide.

- 4. (Currently Amended) Process according to Claim 1, in which the an enzyme of said enzymatic incorporation is the Klenow fragment of DNA polymerase.
- 5. (Currently Amended) Process according to Claim 1, in which the <u>an</u> enzyme <u>of</u> said enzymatic incorporation is selected from the group consisting of a heat-resistant polymerase of a Thermophilus bacterium, a or terminal transferase <u>and</u> or reverse transcriptase.
- 6. (Currently Amended) Process according to Claim 1, in which the nucleic base is a natural nucleic base <u>selected from the group consisting of ehosen from</u> adenine, guanine, cytosine, thymine, uracil, xanthine, hypoxanthine and 2-aminopurine, and derivatives thereof.
- 7. (Currently Amended) Process according to Claim 1, in which R¹ is selected from the group consisting of corresponds to one of the following formulae:



- 8. (Currently Amended) Process according to Claim 1, in which the label is <u>selected</u> from the group consisting of chosen from radioactive products, luminescent products, electroluminescent and fluorescent products, molecules capable of coupling with other molecules, molecules which allow interactions of the antigen-antibody type, and enzymatic labels.
- 9. (Currently Amended) Process according to Claim-1_8, in which R³ the label is a fluorophore.
- 10. (Currently Amended) Process according to Claim 9, in which R³ is selected from the group consisting of ehosen from fluorescein derivatives, biotin derivatives and rhodamine derivatives.
- 11. (Currently Amended) Process according to Claim 1, in which the <u>nucleotide</u> derivative, the <u>modified morpholino-nucleotide</u> or the chain terminator is compound (I) in <u>monophosphate form</u> which m is 0.
 - 12. (Currently Amended) Morpholino-nucleotide corresponding to the formula:



HO
$$\stackrel{\text{O}}{\underset{\text{P}}{\longrightarrow}}$$
 O $\stackrel{\text{O}}{\underset{\text{P}}{\longrightarrow}}$ O $\stackrel{\text{P}}{\underset{\text{OH}}{\longrightarrow}}$ O $\stackrel{\text{P}}{\underset{\text{OH}}{\longrightarrow}}$ O $\stackrel{\text{P}}{\underset{\text{N}}{\longrightarrow}}$ (I)

in which R¹ is adenine and R² represents -CH₂-COOH, -(CH₂)₄-NH₂ or -(CH₂)₄-NH-R³ with wherein R³ representing a group derived from is fluorescein.

13. (Currently Amended) Morpholino-nucleotide of formula:

in which R¹ is thymine and R² represents -CH₂-COOH, -(CH₂)₄-NH₂ or -(CH₂)₄-NH-R³ with wherein R³ representing a group derived from is fluorescein.

14. (Currently Amended) Morpholino-nucleotide corresponding to the formula:



in which R^1 is cytosine and R^2 represents - CH_2 -COOH, - $(CH_2)_4$ -NH₂ or - $(CH_2)_4$ -NH-R³ with-wherein R^3 representing a group derived from is fluorescein.

15. (Currently Amended) Morpholino-nucleotide corresponding to the formula:

HO
$$\stackrel{O}{=}$$
 $\stackrel{O}{=}$ $\stackrel{O}{=}$ $\stackrel{O}{=}$ $\stackrel{O}{=}$ $\stackrel{O}{=}$ $\stackrel{P}{=}$ $\stackrel{O}{=}$ $\stackrel{P}{=}$ $\stackrel{O}{=}$ $\stackrel{R^1}{=}$ $\stackrel{O}{=}$ $\stackrel{R^1}{=}$ $\stackrel{O}{=}$ $\stackrel{P}{=}$ $\stackrel{P}{=}$ $\stackrel{O}{=}$ $\stackrel{P}{=}$ $\stackrel{P}{=}$

in which R¹ is guanine and R² represents -CH₂-COOH, -(CH₂)₄-NH₂ or -(CH₂)₄-NH-R³ with-wherein R³ representing a group derived from is fluorescein.

16. (Currently Amended) Process for manufacturing a morpholino-nucleotide of formula (I):

HO
$$\stackrel{O}{\underset{P}{\longrightarrow}}$$
 O $\stackrel{O}{\underset{P}{\longrightarrow}}$ O $\stackrel{O}{\underset{P}{\longrightarrow}}$ O $\stackrel{P}{\underset{P}{\longrightarrow}}$ O $\stackrel{P}{\underset{R^2}{\longrightarrow}}$ (I)

in which R¹ represents a nucleic base and R² is selected from the represents a group consisting of corresponding to one of the following formulae:

in which n is an integer ranging from 1 to 12 and R³ is selected from the a group consisting of derived from a label, from a protein, from an enzyme, and from a fatty acid or from a peptide,

said process comprising the reaction of

a) reacting a nucleoside triphosphate of formula (II):

wherein in which R^1 has the meaning given above, with a periodate, a compound of formula R^2 NH_2 in which R^2 has the meaning given above R^2 NH_2 , wherein R^2 is selected from the group consisting of:



-(CH₂)_n-NH₂ -(CH₂)_n-SH

 $-(CH_2)_n$ -COOH and $-(CH_2)_n$ -OH,

and sodium borohydride to form a morpholino-nucleotide of formula (III):

wherein R2' has the meaning given above;

- b) isolating the morpholino-nucleotide of formula (III); and
- c) attaching to the morpholino-nucleotide of formula (III) the label, the enzyme and the fatty acid to form the morpholino-nucleotide of formula (I).

17. (Cancelled)

- 18. (Currently Amended) Process according to claim 2, in which the an enzyme of said enzymatic incorporation is the Klenow fragment of DNA polymerase.
- 19. (Currently Amended) Process according to Claim 3, in which the <u>an</u> enzyme <u>of</u> said technique of enzymatic polymerization is the Klenow fragment of DNA polymerase.
- 20. (Currently Amended) Process according to Claim 2, in which the an enzyme of said enzymatic incorporation is selected from the group consisting of a heat-resistant polymerase of a Thermophilus bacterium, a or terminal transferase and or reverse transcriptase.
- 21. (Currently Amended) Process according to Claim 3, in which the <u>an</u> enzyme <u>of</u> said technique of enzymatic polymerization is selected from the group consisting of a heat-resistant polymerase of a Thermophilus bacterium, <u>a</u> or terminal transferase <u>and</u> or reverse

transcriptase.

- 22. (Currently Amended) Process according to Claim 2 in which the nucleic base is a natural nucleic base selected from the group consisting of ehosen from adenine, guanine, cytosine, thymine, uracil, xanthine, hypoxanthine and 2-aminopurine, and derivatives thereof.
- 23. (Currently Amended) Process according to Claim 3 in which the nucleic base is a natural nucleic base <u>selected from the group consisting of ehosen from</u> adenine, guanine, cytosine, thymine, uracil, xanthine, hypoxanthine and 2-aminopurine, and derivatives thereof.
- 24. (Currently Amended) Process according to Claim 2 in which R¹ is <u>selected from</u> the group consisting of corresponds to one of the following formulae:

$$H_3C$$
 NH_2
 NH_2

25. (Currently Amended) Process according to Claim 3 in which R¹ is selected from the group consisting of corresponds to one of the following formulae:

Application Serial No. 09/914,221 Attorney's Docket No. 025219-342

- 26. (Currently Amended) Process according to Claim 2, in which the label is selected from the group consisting of ehosen from radioactive products, luminescent products, electroluminescent and fluorescent products, molecules capable of coupling with other molecules, molecules which allow interactions of the antigen-antibody type, and enzymatic labels.
- 27. (Currently Amended) Process according to Claim 3, in which the label is <u>selected</u> from the group consisting of chosen from radioactive products, luminescent products, electroluminescent and fluorescent products, molecules capable of coupling with other molecules, molecules which allow interactions of the antigen-antibody type, and enzymatic labels.
 - 28. (Original) Process according to Claim 2, in which R³ is a fluorophore.
 - 29. (Original) Process according to Claim 3, in which R³ is a fluorophore.90
- 30. (Currently Amended) Process according to Claim 28, in which R³ is selected from the group consisting of chosen from fluorescein derivatives, biotin derivatives and rhodamine derivatives.
- 31. (Currently Amended) Process according to Claim 29, in which R³ is selected from the group consisting of ehosen from fluorescein derivatives, biotin derivatives and rhodamine derivatives.
- 32. (Currently Amended) Process according to Claim 2, in which the derivative, the modified morpholino-nucleotide or the chain terminator is compound (I) in monophosphate form which m is 0.
 - 33. (Currently Amended) Process according to Claim 3, in which the derivative, the







modified morpholino-nucleotide or said at least one of the chain terminators is compound (I) in monophosphate form which m is 0.